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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,627	10/29/2001	Peter Kratzch	RDID00112CIPUS	6179
7590	12/16/2004		EXAMINER	
BRADFORD G ADDISON BARNES & THORNBURG 11 SOUTH MERIDIAN STREET INDIANAPOLIS, IN 46204			PATTERSON, CHARLES L JR	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/082,627	KRATZCH ET AL.
	Examiner Charles L. Patterson, Jr.	Art Unit 1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 20 September 2004.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-29 is/are rejected.
- 7) Claim(s) 30 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____. |

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Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

The specification is objected to as not complying with 37 CFR § 1.121(b). The instant rule requires that amendments to the specification be made by "adding, deleting or replacing a paragraph, by replacing a section, or by a substitute specification". In the instant amendment, applicants attempt to replace only lines 22-24 of the last paragraph on page 1.

Claim 30 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should not depend to another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits. As stated previously, claim 30 depends from another multiple dependent claim, namely claim 28. Applicants corrected the reference to more than one claim in claims 28-30 but did not address the problem indicated *supra*.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mutants from specific PQQ-dependent glucose dehydrogenase having particular changes in the amino acid sequence, does not reasonably provide enablement for claims of the scope of the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the

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invention commensurate in scope with these claims make and/or use the claimed invention. This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that the instant claims are enabled because the specification teaches how to isolate, mutate and test strains for mutant enzymes having specific properties. They further argue that the enzyme from *A. baumannii* shows significant homology with that from *A. calcoaceticus* and that PQQ-dependent s-GDHs have been found only in the periplasmic space of *Acinetobacter* strains, which tends to suggest a highly conserved amino acid sequence among *Acinetobacter* strains. Finally they argue that "several as yet uncharacterized proteins from [other organisms]...are closely related to *A. calcoaceticus* s-GDH" and that they "likely" have similar structures and catalyze similar reactions.

To start with, it is not seen how being found in the periplasmic space suggests a highly conserved amino acid sequence among *Acinetobacter* strains. Applicants are claiming mutant forms of an enzyme that have "at least two-fold increased substrate specificity for glucose, as compared to at least one other selected sugar substrate" (claim 1) or other specific differences in substrate specificity. Presumably applicants believe that there is not any inventive contribution in isolating PQQ-dependent s-GDHs mutant proteins that have specific properties and that if the methods of doing this are given in the specification, this is sufficient enablement. The examiner does not agree. Table 1 shows the results obtained from specific mutations of the protein from an *Acinetobacter calcoaceticus* strain. Some of these mutant proteins meet the requirements of the instant claims and some do not. As stated previously, exactly what affect a change in a particular amino acid,

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or the corresponding polynucleotide encoding it, will have on an enzyme's activity is not predictable with any certainty. Therefore it is maintained that the specification does not teach one of ordinary skill in the art to obtain mutant strains of the scope of the instant claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7 and 22-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Sode (4). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

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Applicants argue that the claims are limited to the soluble form of GDH and that the reference teaches the membrane-bound form. The examiner has found where it is taught at least in the first paragraph of the Introduction that the enzyme of Cleton-James is the membrane-bound form and that rejection has been dropped. However, in a perusal of Sode the examiner has not found a teaching that this enzyme is the membrane-bound form and therefore the rejection is maintained over this reference. If applicants can point out where it is taught in this reference that it is a membrane-bound form then he will drop the rejection over this reference as well.

Claims 1-7 and 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sode (4). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

This rejection is maintained for the reasons discussed *supra* for the 102 rejection.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Cleton-Jansen, et al. (15). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that the instant reference teaches that "strain PP2403 harbors an insertion mutation in the gene for GDH-B" and that "soluble PQQ-dependent glucose dehydrogenase [is] designated GDH-B". They further argue that PP2403...[is] a mutant strain wherein glucose oxidation is attributable to membrane-bound PQQ-dependent glucose dehydrogenase activity, not to soluble PQQ-dependent glucose dehydrogenase activity". This is not agreed with. As

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stated by applicants "strain PP2403 harbors an insertion mutation in the gene for GDH-B", the soluble PQQ enzyme. Since the enzyme is a mutant of the soluble enzyme and since the activity against glucose is "at least two-fold increased" for glucose as compared to at least one other sugar, the reference meets the requirements of the instant claims.

Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Murphy, et al. (V). The instant reference teaches a protein with SEQ ID NO:1 where XAA is not threonine. This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that "[a] mutant protein of PQQ-dependent s-GDH..." is a claim element and that the instant reference has nothing to do with this protein. In the instant claim, applicants are claiming "[a] mutant protein of PQQ-dependent s-GDH comprising the amino acid sequence..." The claim does not indicate that the mutant protein has any enzymatic activity. One could mutate PQQ-dependent s-GDH by changing all of the residues except for the indicated peptide to those of the instant reference and this protein would meet the requirements of the instant claim.

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Kaneko, et al. (W). The instant reference teaches a protein with SEQ ID NO:2 where XAA is not asparagine. This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

The applicants are correct in that the rejection should have cited Kaneko, et al. (W), as was indicated on the PTO-892. Applicants argue that "[a]

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mutant protein of PQQ-dependent s-GDH..." is a claim element and that the instant reference has nothing to do with this protein. In the instant claim, applicants are claiming "[a] mutant protein of PQQ-dependent s-GDH comprising the amino acid sequence..." The claim does not indicate that the mutant protein has any enzymatic activity. One could mutate PQQ-dependent s-GDH by changing all of the residues except for the indicated peptide to those of the instant reference and this protein would meet the requirements of the instant claim.

Claims 20-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Granger, et al. (X). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that "[a] mutant protein of PQQ-dependent s-GDH..." is a claim element and that the instant reference has nothing to do with this protein. In the instant claim, applicants are claiming "[a] mutant protein of PQQ-dependent s-GDH comprising the amino acid sequence..." The claim does not indicate that the mutant protein has any enzymatic activity. One could mutate PQQ-dependent s-GDH by changing all of the residues except for the indicated peptide to those of the instant reference and this protein would meet the requirements of the instant claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 571-272-0936. The examiner can normally be reached on Monday - Friday from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the

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Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
December 13, 2004